

THE MASS SPECTRA OF 2-ALKYL N-METHYL PYRROLIDINES

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(Received 18 April 1969; accepted 16 June 1969)

Abstract—The mass spectra of a series of 2-alkyl N-methyl pyrrolidines have been examined and fragments which may be pyrrole type structures are apparent. These ions are most prominent in the spectra of the long chain alkyl derivatives.

THE MOST prominent feature of the mass spectra of pyrrolidines, in the few cases documented,¹ is predictably the presence of ions that arise from cleavage at the α carbon. The major ions in the spectrum of pyrrolidine have been rationalized on this basis.¹ In the mass spectrum of proline ethyl ester (I) the base peak (m/e 70) is derived from the loss of the carboethoxy group.² The loss of the α pyridyl substituent upon electron bombardment of nicotine (II) accounts for the base peak (m/e 84) in its spectrum.¹ Aside from these examples, the literature contains little information regarding the mass spectral fragmentation of pyrrolidine derivatives.

Recently we prepared a series of 2-alkyl substituted N-methyl pyrrolidines (IIIa to IIIh) and examined their mass spectral fragmentation patterns. Although cleavage at the α carbon remains an important process upon electron-impact, a previously uninvestigated fragmentation pathway involving the pyrrolidine nucleus has been observed. This alternate path apparently accounts for many of the prominent peaks in the spectra of the long chain alkyl derivatives. We have conducted a deuterium labeling study in an attempt to elucidate the structure of the ions formed via this pathway.

RESULTS AND DISCUSSION

The mass spectral fragmentation data for a series of 2-alkyl N-methyl pyrrolidines (IIIa to IIIh) are listed in Table 1. A rationale for the fragmentation of the ethyl derivative IIIb, consistent with literature proposals,¹ is shown in Scheme 1 (in this study we will focus attention on the formation and structure of ions containing the elements of the pyrrolidine nucleus and neglect in our discussion those ions which can only be derived by destruction of the ring, i.e. those below m/e 70). The base peak is

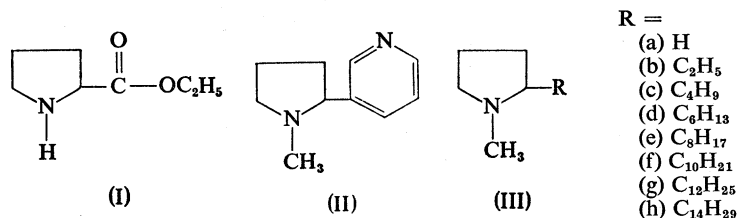


TABLE 1. MASS SPECTRA OF 2-ALKYL N-METHYL PYRROLIDINES

(IIIa)	<i>m/e</i>	55	57	67	69	70	81	82	83	84	85
	%	14	70	5	2	2	0.02	10	1	100	60
(IIIb)	<i>m/e</i>	55	57	70	82	84	94	95	98	109	110
	%	4	2.5	8.5	10	100	0.48	0.5	1.2	1.4	2.5
	<i>m/e</i>	111	112	113							
	%	1.5	2.4	2							
(IIIc)	<i>m/e</i>	55	57	67	69	70	82	84	94	95	98
	%	9	3	1.5	2	3	5	100	1.0	0.2	1.0
	<i>m/e</i>	110	112	137	138	139	140	141			
	%	1.3	0.5	0.15	0.1	0.2	1.0	0.8			
(IIId)	<i>m/e</i>	55	57	67	69	70	82	84	94	95	98
	%	8	5	2	2.5	2.3	4.5	100	5	1.5	0.7
	<i>m/e</i>	108	110	165	166	167	168	169			
	%	0.7	2.3	2.5	0.5	0.3	0.5	0.3			
(IIIe)	<i>m/e</i>	55	57	67	69	70	82	84	94	95	98
	%	5	1.5	1.4	1.4	1.8	5.4	100	10	2.2	1.3
	<i>m/e</i>	108	110	120	136	193	194	195	196	197	
	%	1	7	0.3	0.5	0.5	0.1	0.3	0.3	0.05	
(IIIf)	<i>m/e</i>	55	57	67	69	70	82	84	94	95	98
	%	18	15	3.5	4	3.8	5.7	100	35	12	2.5
	<i>m/e</i>	108	110	120	136	150	164	178	221	222	223
	%	4	5.5	0.7	0.9	0.3	0.2	0.3	1.2	0.3	0.1
	<i>m/e</i>	224	225								
	%	0.2	0.03								
(IIIg)	<i>m/e</i>	55	57	67	69	70	82	84	94	95	98
	%	7.5	3.0	1.9	1.7	1.4	6.7	100	50	13	1.0
	<i>m/e</i>	108	110	120	136	150	206	220	234	249	250
	%	4.5	14	1.0	1.8	0.4	0.3	0.15	0.05	1.5	0.5
	<i>m/e</i>	251	252	253							
	%	0.4	0.3	0.05							
(IIIh)	<i>m/e</i>	55	57	67	69	70	82	84	94	95	98
	%	12	10	2.7	2.4	1.8	7	70	100	30	2.4
	<i>m/e</i>	108	110	120	136	150	220	234	248	262	277
	%	10	12	3	3.1	0.7	0.3	0.4	0.3	0.3	2.5
	<i>m/e</i>	278	279	280							
	%	0.7	0.3	0.2							

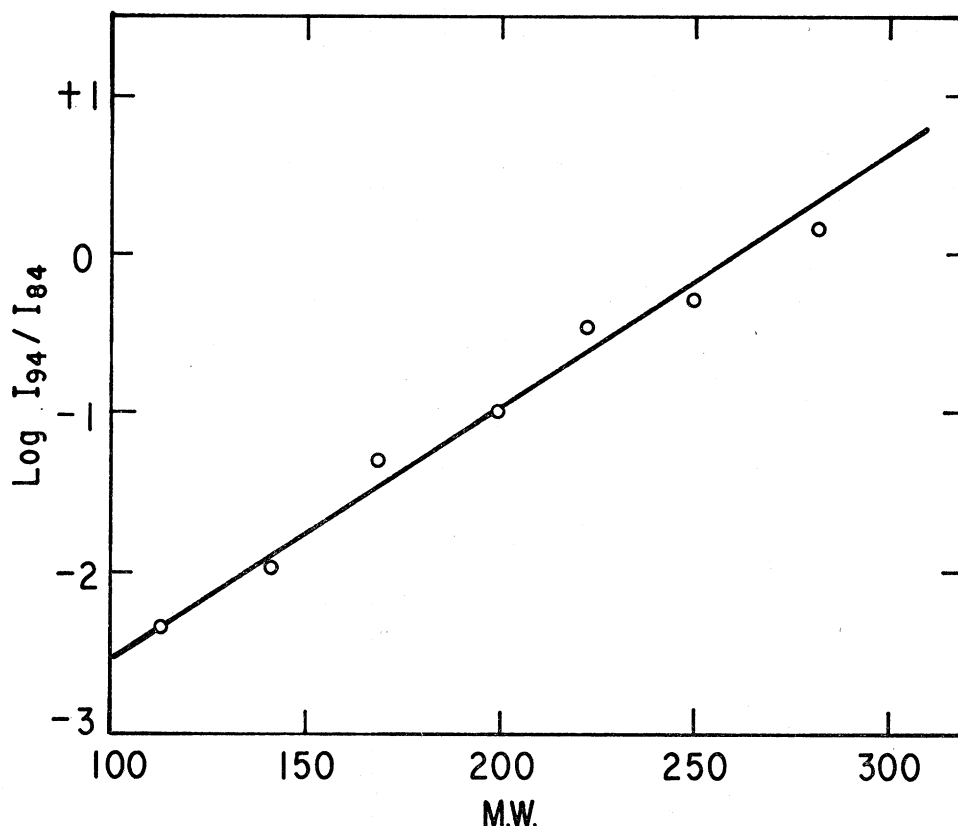
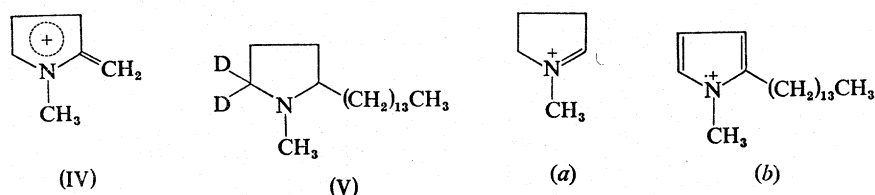


FIG. 1. Change in relative intensity m/e 94 to m/e 84 with increasing side chain length.

at m/e 84 which corresponds to the ion formed by loss of the ethyl group. In the molecular ion region the most prominent peaks beside the molecular ion correspond to ions formed by the loss of one or three hydrogens. The mass spectrum of IIIb is representative of the general fragmentation pattern one observes for the lower members of the series (IIIa to IIIId). As the molecular weight of the alkyl substituent increases other features become apparent in the mass spectrum. The most dramatic change is noted in the steady increase in the intensity of m/e 94 relative to m/e 84 (see Fig. 1). This ultimately results in a situation wherein the base peak in the spectrum of the tetradecyl derivative (IIIh) is at m/e 94 rather than m/e 84. The molecular ion region in the spectra of the higher members of the series is also markedly different from the molecular ion region of the lower members in the series; the most prominent peak in this part of the spectrum for compounds IIIId to IIIh is $[M - 4]$ rather than $[M]$, $[M - 1]$ or $[M - 3]$. Finally, in the spectra of IIIe to IIIh there are peaks corresponding to the loss of 19, 33, 47 etc. mass units from the molecular ion.

From these results we have rationalized the fragmentation pattern of the tetradecyl derivative as shown in Scheme 2, the spectrum of this compound being generally representative of the latter members of the series. We believe the differences in the fragmentation pattern observed within series III, other than fragments arising from

the side chain, are due to the formation of pyrrole type ions in relatively abundant concentrations upon electron-impact of the long chain alkyl derivatives. We have postulated, as the structure of $[M - 4]$, an odd electron N-methyl pyrrole ion. The ions corresponding to $[M - 19]$, $[M - 33]$, etc. are envisioned as even electron species formed by the loss of an alkyl radical (methyl, ethyl, etc.) from the pyrrole $[M - 4]$ ion; these ions are of relatively low intensity but are the most intense ions in this portion of the spectrum and therefore they are quite prominent. On the basis of this reasoning, the ion at m/e 94, which is the base peak in the spectrum of IIIh, would have the proposed structure IV which should be reasonably stable (this ion may be somewhat analagous to the tropylium ion). Although the structures of these ions are speculative, as they must be without knowledge of information such as appearance potentials, we have attempted to gain some insight as to the structure of the ions in question by deuterium labeling.



For this study we have prepared 5,5 dideutero-2-tetradecyl N-methyl pyrrolidine (V). Preparation of other deuterated compounds, although desirable, was beyond the scope of our present investigation. The mass spectrum of V and the corresponding undeuterated compound, IIIh, are shown in Fig. 2. The expected m/e values for the ions derived from the deuterated compound via the proposed fragmentation pattern are given in parenthesis in Scheme 2. The results for the mass spectral fragmentation of the deuterated compound are not in complete agreement with these predictions. As expected m/e 84 (ion VI) is shifted to m/e 86 in the spectrum of the deuterated compound V; however, structures that we have postulated as pyrrole type ions are formed with an unexpectedly high loss of both deuteriums. For example, $[M - 6]$ (the loss of 2 hydrogens and 2 deuteriums) is a more intense ion than $[M - 5]$ (loss of 3 hydrogens and 1 deuterium); also m/e 94 (proposed structure IV) in the spectrum of IIIh is only partially shifted to m/e 95 in the spectrum of V, the most intense ion still being m/e 94.*

Although the extent of loss of both deuteriums was unexpected, the mass spectrum of V confirms the fact that deuterium, prior to electron-impact was bonded to ring carbons. If deuterium had scrambled into the side chain during synthesis (which is unlikely from what is known about the mechanism of the reactions involved)³ we would not see the degree of shifting of m/e 84 to m/e 86. Also, random hydrogen-deuterium exchange after electron-impact but before hydrogen/deuterium loss is inconsistent with the highly specific loss of deuterium observed, especially in the molecular ion region. Finally, deuterium scrambling to a specific site in the alkyl

* The loss of both deuteriums in m/e 94 can be rationalized by deuterium scrambling involving the side chain; however, such an argument cannot be used in explaining the preferred loss of 2 deuteriums $[M - 6]$ over 1 deuterium $[M - 5]$ from the molecular ion.

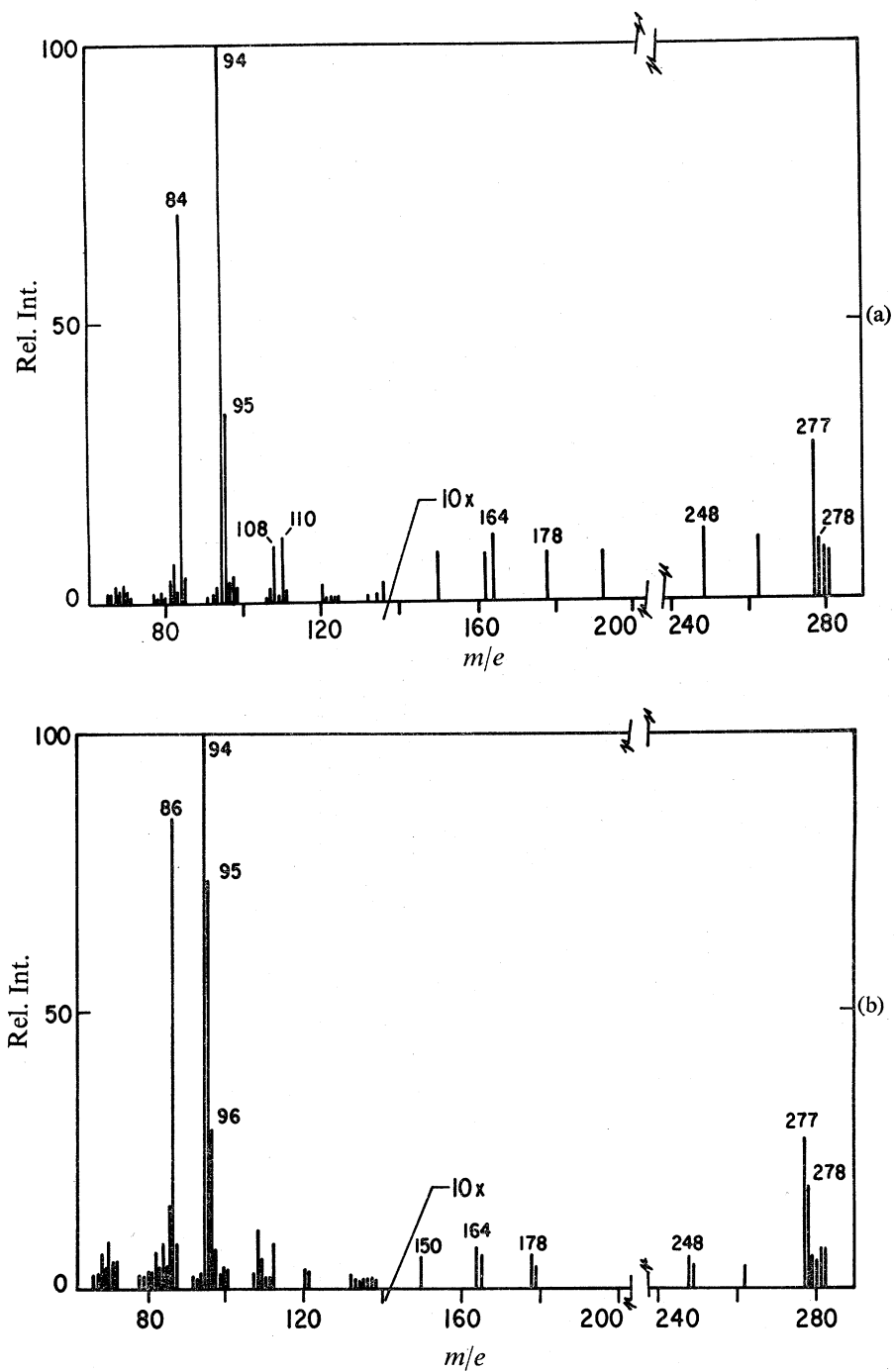


FIG. 2. Mass spectra of 2-tetradecyl N-methyl pyrrolidine (a) and 5,5-dideutero-2-tetradecyl N-methyl pyrrolidine (b).

chain followed by facile loss of this deuterium seems highly unlikely. There are no indications from fragments apparently derived by cleavage of the alkyl chain (i.e. loss of methyl, ethyl, propyl, etc.) to support such an argument. The loss of deuterium upon electron-impact therefore strongly indicates that the process responsible for the formation of $[M - 4]$ ions in the undeuterated compounds involves cleavage of hydrogens attached to ring carbons. The unusually high loss of both deuteriums, which does not invalidate this hypothesis, requires further investigation.

It would be of interest to see what elements of the spectra of these pyrrolidine compounds are analogous to the spectra of the corresponding N-methyl pyrrole derivatives; however, these spectra are unavailable. The spectrum of 2-methyl pyrrole, which has been reported,⁴ has as its base peak an $[M - 1]$ ion for which the proposed structure is similar to IV.

What role the alkyl substituent plays in the fragmentation process responsible for these pyrrole ions is not clear. Applying generally accepted assumptions about electron bombardment fragmentation processes we would expect, in all cases, the formation of the even electron ion (*a*) and an alkyl radical to be the most favorable fragmentation path, as indeed it may well be even for the tetradecyl derivative. An ion such as *b* which has aromatic character may become more important as the alkyl group increases in length due to the greater distribution of energy within the ion that such a change might imply. Such a change in fragmentation pattern would most dramatically be observed in the change in intensity of m/e 94 (IV) which should be a highly stable ion. It should be emphasized that this explanation is merely speculative and we hope, through future experiments, to clarify the role of the substituent in directing the fragmentation process in the pyrrolidine ring.

The possibility that the formation of pyrrole ions is a thermal process seems unlikely. All the compounds were subjected to the same inlet and source temperatures. We have also introduced the 2-dodecyl derivative into the mass spectrometer at inlet temperatures ranging from 150°C to 220°C without observing any noticeable change in its spectrum.

We plan to determine the importance of the loss of hydrogen to form 'aromatic ions' in the mass spectral fragmentation of analogous tetrahydrofuran and tetrahydrothiophene derivatives.*

EXPERIMENTAL

The N-methyl pyrrolidines were prepared from their acyclic counterparts by photocyclization of the N-chloro derivatives under conditions of Hofmann Loeffler reaction.⁶ (The 5,5 dideutero pyrrolidine (V) was prepared from the corresponding deuterated amine prepared by LiAlD_4 reduction of N-methyl stearamide. The incorporation of 2 deuteriums into the amine was estimated to be $\geq 95\%$ by mass spectral analysis.) All compounds in this study have been reported^{6,7,8} except for 2-hexyl, 2-octyl and 2-decyl derivatives for which the following analytical results are given:

2-hexyl N-methyl pyrrolidine picrate. Found: C, 51.39; H, 7.18. $\text{C}_{17}\text{H}_{26}\text{N}_4\text{O}_7$ requires C, 51.25; H, 6.73%.

2-octyl N-methyl pyrrolidine picrate. Found: C, 53.97; H, 7.47. $\text{C}_{19}\text{H}_{30}\text{N}_4\text{O}_7$ requires C, 53.52; H, 7.04%.

2-decyl N-methyl pyrrolidine picrate. Found: C, 55.32; H, 8.03. $\text{C}_{21}\text{H}_{34}\text{N}_4\text{O}_7$ requires C, 55.51; H, 7.49%.

* Aromatization by the loss of 4 hydrogens has been observed in the mass spectrum of 1, 2, 3, 4 tetrahydrobenzothiophene⁵ to give a fully aromatic system.

All compounds were purified by preparative gas chromatography on a Carbowax 20 M column (5' \times $\frac{1}{8}$ "). The purified samples were checked for the presence of pyrrole or other amine impurities by i.r. and u.v. spectroscopy.

Mass spectra were obtained on a CEC Model 103 mass spectrometer. The ionization voltage was 70 eV. Inlet temperatures for all samples were approximately 200°C. For 2-dodecyl N-methyl pyrrolidine spectra were obtained on samples introduced at inlet temperatures of 150°C, 175°C, 220°C as well as 200°C.

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